



[Billing Code 4140-01-P]

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### NATIONAL INSTITUTES OF HEALTH

#### Announcement of Requirements and Registration for “Follow that Cell” Challenge

**AUTHORITY:** 15 U.S.C. 3719

**SUMMARY:** Through the “Follow that Cell” Challenge (the “Challenge”), the Single Cell Analysis Program (SCAP) - <http://commonfund.nih.gov/Singlecell/index>, a component of the National Institutes of Health Common Fund - <http://commonfund.nih.gov/about>, is searching for novel methods for analyzing dynamic states of individual cells that can serve as the basis for predicting alterations in cell behavior and function over time. The goal of the Challenge is to develop new tools and methods that allow time-dependent measurements at the single-cell level in a complex tissue environment in order to assess functional changes, provide information on the health status of a given cell, and help guide diagnosis and therapeutic treatments related to human disease states. Technological breakthroughs in this arena could allow researchers and physicians to identify rare cells in a mixed population, such as individual cells that can transform and become cancerous, cells that are latently infected with a pathogenic virus, or cells that develop resistance to drugs over time.

The NIH Common Fund currently supports SCAP grants, the majority of which are associated with academic institutions. This Challenge, structured in two phases, will

strengthen and complement the existing SCAP grant portfolio by reaching out to a more diverse population of innovators and solvers, including not only those who are from academic institutions but also those who are from research and development communities in the private sector and those who are outside biomedical disciplines. The NIH believes this Challenge will stimulate investment from both public and private sectors in single-cell analysis research and product development, which, in turn, could lead to the development of more sensitive, robust, and cost-effective assay approaches, reagents, tools, and devices for basic research and clinical diagnosis.

**DATES:** Phase 1: Effective on August 15, 2014

Phase 1 Submission period ends: December 15, 2014, 11:59 p.m. ET

Phase 1 Judging Period: December 16, 2014, to February 16, 2015

Phase 1 Winners and other Finalists Announced: March 16, 2015

Phase 2 begins: March 17, 2015

Phase 2 Submission period ends: March 30, 2017, 11:59 p.m. ET

Phase 2 Judging Period: March 31, 2017, to June 30, 2017

Phase 2 Winners announced: July 31, 2017

The NIH may shorten the submission period for Phase 2 and adjust dates for judging and winner(s) announcement if the Phase 1 winners' feasibility assessments suggest a shorter Phase 2 submission period is possible. The NIH will announce any changes to the timeline by amending this *Federal Register* notice no later than March 16, 2015. This Challenge will be administered by InnoCentive, Inc., on behalf of the NIH [www.innocentive.com/followthatcell](http://www.innocentive.com/followthatcell).

**FOR FURTHER INFORMATION CONTACT:** Yong Yao, Ph.D., NIH, 301-443-6102; or Erin Shannon, NIH, 301-443-3959.

**SUPPLEMENTARY INFORMATION:**

**Subject of Challenge:**

Many biological experiments are performed under the assumption that all cells of a particular “type” are identical. However, recent data suggest that individual cells within a single population may differ quite significantly, and these differences can drive the health and function of the entire cell population. Single-cell analysis comprises a broad field that covers advanced optical, electrochemical, mass spectrometry instrumentation, and sensor technology, as well as separation and sequencing techniques. Although the approaches currently in use can offer snapshots of single cells, the methods are often not amenable to longitudinal studies that monitor changes in individual cells *in situ*.

In this Challenge, the NIH is seeking novel robust methods for analysis of individual cells that can detect and assess changes in cell behavior and function over time, either as a result of natural state changes or when perturbed (e.g., by a drug, biological stimulus, infectious agent, pathological lesion, or mechanical forces). It is hoped that such methods will yield creative and new, yet feasible, solutions for following a single cell over time in a complex multicellular environment to detect changing cell properties, preferably using multiple integrated measures.

Solutions submitted to this Challenge should:

- include measurements or assays that are nondestructive and capable of producing temporal data at the individual cell level starting with eukaryotic cells in a complex/mixed cell population;
- address at least one impactful, biological, or clinical question proposed by the Solver;
- demonstrate robust reproducibility;
- address gaps or deficiencies in current capabilities that may include but are not limited to:
  - Tools that provide significant advances in sensitivity and selectivity in the spatiotemporal resolution of molecules/structures/activities within single cells *in situ* (e.g., high resolution imaging of molecular interactions within single cells, molecular probes that are at least an order of magnitude smaller in size than existing versions of reporter molecules such as fluorescent proteins);
  - Automated and scalable assays to detect meaningful functional changes in single cells in complex tissue environments that improve upon processing time and reduce overall cost; or
  - New combinations of tools and approaches to maximize data generation over several parameters (e.g., proteins, lipids, metabolites, signal secretion/reception/transduction, migratory changes);
- advance what is currently considered the state-of-the-art.

Solutions describing existing, well-established and/or currently supported approaches, especially commonly used strategies are not of interest unless a compelling case is made that significant, quantifiable advances are proposed and/or the methods and measures are used in unique combinations that have not been previously tested together for the analysis of individual cells in complex environments.

We welcome solutions from individuals, teams, and entities from all U.S. sources, including the public sector, private sector, and nonprofit groups.

### **Eligibility Rules for the Challenge**

#### **1. To Participate**

This Challenge is open to any “Solver” where “Solver” is defined as an individual, a group of individuals (i.e., a team), or an entity. Whether singly or as part of a group or entity, each individual participating in the Challenge must be 18 years of age or older.

Eligibility to participate in Phase 2 of the Challenge is conditioned upon participation in Phase 1 of the Challenge and being selected as a “Phase 1 Finalist.” Phase 1 Finalists are any and all Phase 1 prize winners and any individual, team, and/or entity whose solution received a meritorious rating based on the judging criteria.

#### **2. To Win**

To be eligible to win a prize under this Challenge, the Solver --

1. Shall have registered to participate in the Challenge under the process identified at the InnoCentive website  
[www.innocentive.com/followthatcell](http://www.innocentive.com/followthatcell).

2. Shall have complied with all the requirements under this section on Eligibility.
3. In the case of a private entity, shall be incorporated in and maintain a primary place of business in the United States; and in the case of an individual, whether participating singly or in a group, shall be a citizen or permanent resident of the United States. *Note:* Non-U.S. citizens and nonpermanent residents can participate as a member of a team that otherwise satisfies the eligibility criteria but will not be eligible to win a monetary prize (in whole or in part); however, their participation as part of a winning team, if applicable, may be recognized when results are announced.
4. In the case of an individual, he/she may not be an employee of the NIH; an individual involved in formulation of the Challenge and/or serving on the technical evaluation panel; any other individual involved with the design, production, execution, distribution, or evaluation of this Challenge; or members of the individual's immediate family (specifically, a parent, step-parent, spouse, domestic partner, child, sibling, or step-sibling).
5. An individual, team, or entity that is currently on the Excluded Parties List (<https://www.epls.gov/>) will not be selected as a Finalist or prize winner.
6. In the case of an entity, may not be a federal entity; and in the case of an individual, may not be a federal employee acting within the scope of his or her employment.

7. Federal employees otherwise permitted to participate in the Challenge shall not work on their submission during assigned duty hours. *Note:* Federal ethical conduct rules may restrict or prohibit federal employees from engaging in certain outside activities, so any federal employee not excluded under the prior paragraph seeking to participate in this Challenge outside the scope of employment should consult his/her agency's ethics official prior to developing a submission.
8. Federal grantees may not use federal funds to develop Challenge submissions.
9. Federal contractors may not use federal funds from a contract to develop Challenge submissions or to fund efforts in support of a Challenge submission.
10. An individual shall not be deemed ineligible to win because the individual used federal facilities or consulted with federal employees during the Challenge provided that such facilities and/or employees, as applicable, are made available on an equitable basis to all individuals and teams participating in the Challenge.

All questions regarding the Challenge should be directed to Dr. Yao or Ms. Shannon, identified above, and answers will be posted and updated as necessary at [www.innocentive.com/followthatcell](http://www.innocentive.com/followthatcell) under Frequently Asked Questions. Questions from Solvers that may reveal proprietary information related to solutions under development may be addressed in the InnoCentive project room, an online secure and confidential communication forum.

## Submission Requirements

The Challenge has two phases.

**Phase 1 (Theoretical)** - Phase 1 of the Challenge requires a written proposed solution which describes a novel method for analyzing dynamic states of individual cells that can serve as the basis for predicting alterations in cell behavior and function over time.

The Phase 1 Submission shall include:

1. A comprehensive description of the proposed solution in 10 pages or less, 8.5x11 inch page, 10-point font or greater and one inch margins including:
  - a. A one-paragraph executive summary that clearly states the biological or clinical question to be solved;
  - b. Background information supporting the significance of the biological or clinical question(s) and the proposed approach, pitfalls, and validation scheme that addresses efforts to support reproducibility; if possible, citing selected peer-reviewed articles that strengthen the proposed solution. The full citations for articles should be included in the references section;
  - c. Descriptions of methods and technologies key to implementation; and
  - d. A “State-of-the-Art” Statement that describes approaches currently in use (if any) and clearly explains how the methods and measures proposed advance existing capabilities.
2. A biographical sketch, in no more than four pages, of your experience and relevant expertise required to validate the proposed solution, including



publications, if applicable. Team submissions should include a biosketch for each team member.

3. A feasibility assessment and a statement describing your ability to execute the proposed solution in Phase 2 (Reduction to Practice), including the estimated timeframe, supporting precedents, and any special resource(s) you may have or will need. If relevant, the assessment of feasibility should also address Protections for Humans Subjects, compliance with policies related to the use of vertebrate animals, biosafety issues, and use of methods/technologies covered by patents or other intellectual property protection, as applicable.
4. List of essential materials and reagents including their suppliers, if applicable.
5. Appendices describing existing, unpublished experimental data that support your proposed solution may be included. Please note that while a page limit is not placed on appendices, please be concise in your presentation and include only relevant data in support of your solution.
6. References.

All Phase 1 Solvers will agree to allow the executive summaries of their solutions to be posted on the NIH Common Fund website.

**Phase 2 (Reduction to Practice)** - All Phase 1 Finalists will be eligible to participate as Phase 2 Solvers in the second phase of the Challenge to produce proof-of-concept data. Phase 2 Solvers will execute their proposed solution(s) to Phase 1 of the Challenge and submit (in the Phase 2 submission) single cell data addressing significant biological or clinical question(s) by measuring changes in a single cell over time. Phase 2 Solvers are encouraged to incorporate the expert review feedback from Phase 1 and

form teams/partnerships to improve the likelihood of successful solution implementation. Detailed submission requirements for Phase 2 of the Challenge will be available to Phase 2 Solvers no later than 30 days after the Phase 1 Finalists are announced.

The Phase 2 submission shall include:

1. Project Description: Detailed description of materials, methods, personnel, resources, and schedule.
2. Execution: Successful generation of time course measurements from a single cell based on the Phase 1 solution, which may also include innovations, essential alterations in the proposed plan, and/or trouble-shooting technical or analytical challenges. Any changes from the original design (Phase 1 solution) should be documented and explained.
3. Data: Quality and significance of the time course data produced; efforts to assess reproducibility.

### **Registration and Submission Process for Solvers**

To register and submit for this Challenge, Solvers may access the registration and submission platform from any of the following:

- Access the [www.challenge.gov](http://www.challenge.gov) website and search for “Follow that Cell.”
- Access the NIH Single Cell Analysis website <https://commonfund.nih.gov/Singlecell/index>; a registration link for the Challenge can be found on the landing page under Challenge Description.
- Access the Innocentive Challenge website at [www.innocentive.com/followthatcell](http://www.innocentive.com/followthatcell)

### **Amount of the Prize**

Phase 1: \$100,000

Phase 2: \$400,000

As determined by the judges, up to six prizes may be awarded for Phase 1 solutions from a total prize award pool of \$100,000, and up to 2 prizes may be awarded for Phase 2 solutions from a total pool of \$400,000.

In addition, any and all Phase 1 Finalists will be acknowledged by the NIH Common Fund Single Cell Analysis Program and invited to attend The 3<sup>rd</sup> Annual Single Cell Analysis Investigators Meeting near Bethesda, Maryland, U.S.A., on April 20-21, 2015, during which they may be invited to present their theoretical solution. Any funds for travel reimbursements for Phase 1 winners will be counted within the total prize amounts.

Note that in the event a winning team includes individual members who are neither citizens nor permanent residents of the United States, these individuals are welcome to attend the meeting and their names will be listed among the team members, but they cannot be reimbursed for their travel and related expenses.

The NIH reserves the right to cancel, suspend, and/or modify this Challenge at any time through amendment to this *Federal Register* notice. In addition, the NIH reserves the right to not award any prizes if no solutions are deemed worthy. The award approving official for Phase 1 and Phase 2 of this Challenge is the NIH Principal Deputy Director.

#### **Basis Upon Which Winners Will Be Evaluated**

Solutions for both phases of the Challenge will be evaluated by a Technical Evaluation Panel using the criteria and rating scales describe below. NIH scientific staff

from the various Institutes and Centers (ICs), including the Office of Strategic Coordination, will review highly rated solutions for scientific alignment to the single-cell analysis program, relevance to the NIH mission, and potential overlap with existing projects. The judges, comprising three senior NIH leaders, will use the technical and programmatic evaluations to determine the Phase 1 prize winners, those Solvers in Phase 1 who are deemed meritorious, and the Phase 2 prize winner(s). Prizes will be approved by the NIH Principal Deputy Director.

Phase 1 (Theoretical) – The technical evaluation panel will use the following criteria and rating scales for evaluating proposed solutions with high scores reflecting the mostly highly rated solutions: (maximum 100 points; plus bonus points)

1. Time Course Measurements – Must permit time course measurements on the same cell over a biologically significant period of time rather than a single, snapshot assessment; provide rationale for the functional measure(s) and chosen duration. (0-25 points)
2. Predictability – Approach must provide technical requirements (sensitivity, selectivity, spatiotemporal resolution, signal-to-noise ratio, etc.) that will adequately support robust prediction of phenotypic changes in cell state that occur naturally or in response to controlled perturbation(s). (0-20 points)
3. Cellular Environment – Must pertain to single cells in a complex multicellular environment with preference for cell types that are phylogenetically closer to human (a-d below ordered from highest to lowest in interest). (0-20 points)
  - a. Multicellular living organism (15-20 points)
  - b. Intact tissue (10-15 points)

- c. Organoid culture (5-10 points)
- d. Cell culture (0-5 points)
- 4. Significance – Must address a meaningful biological or clinical question with high potential impact if successful; must advance current capabilities and address issues related to reproducibility. (0-20 points)
- 5. Adaptability – Must describe broad utility and scalability. The approach should lend itself to more than one particular cell type. (0-15 points)

Bonus Points (maximum 50 bonus points)

- Feasibility – Should provide sufficient details to support the feasibility that the proposed solution will be reduced to practice in less than two years, including published or unpublished data, scientific basis, technological capability, and resources. (Bonus up to 30 points)
- Throughput – Methods that describe multiplexed analysis to increase throughput and coverage will be rated more favorably. (Bonus up to 10 points)
- Data Content – Methods that promote the collection and integration of multiple types of data (e.g., biochemical, physiologic, morphological, or ‘omics-level analyses) on individual cells will be rated more favorably. (Bonus up to 10 points)

Phase 2 (Reduction to Practice) – Phase 2 submissions must provide a clear description of how experiments were conducted (including use of appropriate controls, instrument calibration, etc.) and how the data were collected. Phase 2 submissions must include all requisite scientific and technical details including materials, methods,

protocols, and devices to demonstrate successful execution of the proposed solution. It should also document trouble-shooting: what technical or analytical challenges were encountered and how were these resolved? Has reproducibility of the approach been demonstrated? What improvements and/or innovations were implemented above and beyond what was proposed in Phase 1?

The technical evaluation panel will use the following criteria and rating scales for evaluating proposed Phase 2 solutions, with high scores reflecting the mostly highly rated solutions. (maximum 100 points, plus bonus points)

1. Time Course Measurements – Must provide time course measurement data on the same cell over a biologically significant period of time with adequate time intervals. (0-25 points)
2. Predictability – Approach must provide technical specifications (sensitivity, selectivity, spatiotemporal resolution, signal-to-noise ratio, etc.) that will adequately support robust prediction of phenotypic changes in cell state that occur naturally or in response to controlled perturbation(s). The data should also support robustness, stability, and reproducibility of measurements. (0-20 points)
3. Cellular Environment – Must provide measurement data pertaining to single cells in a complex multicellular environment with preference for cell types that are phylogenetically closer to human; (a-d below ordered from greatest to least in interest). (0-20 points)
  - a. Multicellular living organism (15-20 points)
  - b. Intact tissue (10-15 points)
  - c. Organoid culture (5-10 points)

d. Cell culture (0-5 points)

4. Significance – Must address a meaningful biological or clinical question with high potential impact if successful; must make technical advances and/or improvements to existing methods and approaches. Should provide evidence of reproducibility. (0-20 points)
5. Adaptability – Must describe broad utility and scalability. The approach should lend itself to more than one particular cell type. (0-15 points)

Bonus Points (maximum 20 bonus points)

- Throughput Methods that promote multiplexed analysis to increase throughput and coverage will be rated more favorably. (Bonus up to 10 points)
- Data Content Methods that collect and integrate multiple types of data (e.g., biochemical, physiologic, morphological, or ‘omics-level analyses) on individual cells will be rated more favorably. (Bonus up to 10 points)

As part of the evaluation process, the panel may request a demonstration of the technology.

### **Additional Information**

#### Statutory Authority of the Funding Source:

This Challenge is consistent with and advances the mission of the NIH Division of Program Coordination, Planning, and Strategic Initiatives to identify research that represents important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis, including coordination of the NIH Common Fund. The NIH Common Fund was enacted into law by Congress through the 2006 National Institutes of Health Reform Act to support cross-cutting, trans-

NIH programs that require participation by at least two NIH ICs or would otherwise benefit from strategic planning and coordination. The requirements for the NIH Common Fund encourage collaboration across the ICs while providing the NIH with flexibility to determine priorities for Common Fund support. To date, the Common Fund has been used to support a series of short-term, exceptionally high-impact, trans-NIH programs. <http://commonfund.nih.gov/about>

Intellectual Property: By submitting the Submission, each Solver warrants that he or she is the sole author and owner of any copyrightable works that the Submission comprises, that the works are wholly original with the Solver (or is an improved version of an existing work that the Solver has sufficient rights to use and improve), and that the Submission does not infringe any copyright or any other rights of any third party of which Solver is aware.

To receive an award, Solvers will not be required to transfer their exclusive intellectual property rights to the NIH. Instead, Solvers will grant to the federal government a nonexclusive license to practice their solutions and use the materials that describe them. To participate in the Challenge, each Solver must warrant that there are no legal obstacles to providing a nonexclusive license of Solver's rights to the federal government. This license will grant to the United States government a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States throughout the world any invention made by the Solvers that covers the Submission. In addition, the license will grant to the federal government and others acting on its behalf, a paid-up, nonexclusive, irrevocable, worldwide license in any copyrightable works that the Submission comprises, including the right to reproduce,



prepare derivative works, distribute copies to the public, and perform publicly and display publicly said copyrightable works.

Liability and Indemnification: By participating in this Challenge, each Solver agrees to assume any and all risks and waive claims against the federal government and its related entities, except in the case of willful misconduct, for any injury, death, damage, or loss of property, revenue, or profits, whether direct, indirect, or consequential, arising from participation in this Challenge, whether the injury, death, damage, or loss arises through negligence or otherwise. By participating in this Challenge, each Solver agrees to indemnify the federal government against third party claims for damages arising from or related to Challenge activities.

Insurance: Based on the subject matter of the Challenge, the type of work that it will possibly require, as well as an analysis of the likelihood of any claims for death, bodily injury, or property damage, or loss potentially resulting from competition participation, Solvers are not required to obtain liability insurance or demonstrate financial responsibility in order to participate in this Challenge.

Privacy, Data Security, Ethics, and Compliance: Solvers are required to identify and address privacy and security issues in their proposed projects and describe specific solutions for meeting them. In addition to complying with appropriate policies, procedures, and protections for data that ensures all privacy requirements and institutional policies are met, use of data should not allow the identification of the individual from whom the data was collected. Solvers are responsible for compliance with all applicable federal, state, local, and institutional laws, regulations, and policies. These may include, but are not limited to, Health Information Portability and

Accountability Act (HIPAA) protections, Department of Health and Human Services (HHS) Protection of Human Subjects regulations, and Food and Drug Administration (FDA) regulations. If approvals (e.g., from an Institutional Review Board) will be required to initiate project activities in Phase 2, it is recommended that Solvers apply for approval at or before the Phase 1 submission deadline. The following links are intended as a starting point for addressing regulatory requirements but should not be interpreted as a complete list of resources on these issues:

## **HIPAA**

Main link: <http://www.hhs.gov/ocr/privacy/index.html>.

Summary of the HIPAA Privacy Rule:

<http://www.hhs.gov/ocr/privacy/hipaa/understanding/summary/index.html>.

Summary of the HIPAA Security Rule:

<http://www.hhs.gov/ocr/privacy/hipaa/understanding/srsummary.html>.

## **Human Subjects—HHS**

Office for Human Research Protections:

<http://www.hhs.gov/ohrp/index.html>.

Protection of Human Subjects Regulations:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>.

Policy & Guidance:

<http://www.hhs.gov/ohrp/policy/index.html>.

Institutional Review Boards & Assurances:

<http://www.hhs.gov/ohrp/assurances/index.html>.

## **Human Subjects—FDA**

Clinical Trials:

<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm> .

Office of Good Clinical Practice:

<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018191>

## **Consumer Protection—Federal Trade Commission**

Bureau of Consumer Protection:

<http://business.ftc.gov/privacy-and-security> .

## **Challenge Judges:**

Director, Division of Program Coordination, Planning, and Strategic Initiatives, NIH

Director, National Institute of Mental Health

Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB)

## **Acknowledgements**

The National Institutes of Health Single Cell Analysis Program team would like to thank the following Subject Matter Experts for providing guidance to our contractor, InnoCentive, as NIH staff developed this Challenge.

Ronald N. Germain, M.D., Ph.D., NIH, National Institute of Allergy and Infectious Diseases, Laboratory of Systems Biology

Leroy Hood, M.D., Ph.D., President, Institute for Systems Biology

Tom Misteli, Ph.D., NIH, National Cancer Institute, Laboratory of Receptor Biology and Gene Expression

Pamela Gehron Robey, Ph.D., NIH, National Institute of Dental and Craniofacial Research, Craniofacial and Skeletal Diseases Branch

Hari Shroff, Ph.D., NIH, NIBIB, High Resolution Optical Imaging Laboratory

Date: August 4, 2014

---

Lawrence A. Tabak, D.D.S., Ph.D.

Principal Deputy Director

National Institutes of Health

[FR Doc. 2014-18870 Filed 08/08/2014 at 8:45 am; Publication Date: 08/11/2014]